STUDY OF BRAIN WHITE MATTER ANISOTROPY

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Abstract - **An *in vitro* study to detect brain white matter anisotropy is presented. Porcine cylindrical samples were compressed (0,5mm/mn) in a testing apparatus composed of a testing machine combined with a precision balance. Two different types of samples were harvested: 1) cut in parallel and 2) perpendicular to axon fibers present in white matter. For an elongation of 0 to 25% white matter exhibited isotropy. For deformation superior to 25%, the load versus elongation curves diverged increasingly, just to a difference of 37% between the samples of the two perpendicular directions for 35% of elongation, respectively.**

Keywords **– Biomechanics, brain, white matter, compression, anisotropy.**

I. INTRODUCTION

Recent progress in numerical simulation, parallel to improvements in medical imaging allows to implement biomechanical simulation of brain tissue. Those simulations will be useful for prognosis and diagnostic concerning post-traumatic reaction of brain tissue or the development of brain tumors and their effect on intracranial structures.

Simulation, to be realistic, has to take into account the mechanical properties of tissues and even so to consider all basic stresses: compression/traction, shear, and torsion. This motivates detailed investigations of different kinds of tissue under different boundary conditions. In this study we performed experiments to verify the existence of anisotropy in white matter of the brain under compression. Existence of anisotropy would be of high importance for the design and execution of the above mentioned simulations.

Low speed tests on brain tissue have been executed for more than thirty years. During the sixties and seventies, experiments were mainly conducted *in vitro* on animal brain, using cylindrical samples. Most were creep and relaxation tests [1, 2]. Linear viscoelastic models have been used to analyze data [2], or calculate simple viscoelastic parameters as viscosity or elasticity moduli [1, 3].

More recently, Miller et al. [4] conducted compression tests at different speeds (0.005mm/mn, 5mm/mn, 500mm/mn) on swine brains. Results were presented using a non-linear viscoelastic model.

All those past experiments did not take into account brain anisotropy, which is a critical factor in biomechanical simulation of brain. Except Metz [3], all samples used for *in vitro* tests were cylindrical ones, which seems to be the most reliable way to reproduce geometry of samples in such a soft tissue as the white and gray matter of the brain. Due to their axial symmetry cylindrical samples imply axial tests only. Anyway, anisotropy may be investigated by harvesting samples in perpendicular directions, which was the approach chosen for the present work. Experiments consisted of quasistatic compression on porcine cylindrical brain samples.

II. METHODOLOGY

A. Histology

Brain white matter has been chosen for this study aiming for evaluation of tissue anisotropy. Even so extremely soft and fragile this tissue should exhibit anisotropy due to its histological structure. Considering its delicate properties we decided to work with cylindrical probes, since this is the most convenient and reproducible way to harvest samples. To enable brain anisotropy measurements, samples had to be cut into different directions, based on a careful study of the particular brains topography.

Both gray and white matter are mainly composed of glial cells and neurons. While glial cells are present in both tissues, soma and dendrites of the neurons are to be found in gray matter. The major part of the axons forms an important part of the white matter. Since axons are long fibers, anisotropy is more probable in white than in gray matter. Fig.1 shows a schematic view of white and gray matter. The axon fibers coming out from gray matter are forming the white matter. Orientations chosen for the cut out of the cylindrical samples are also indicated.

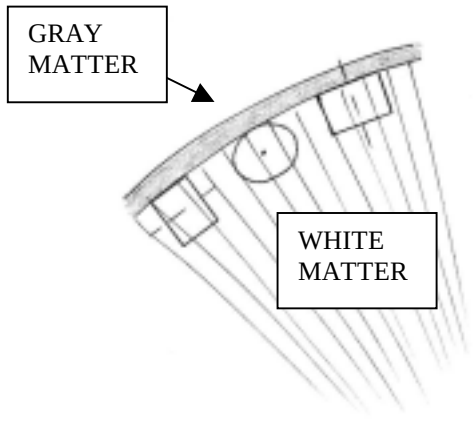

Fig. 1 : Sites and ways of sample cutting in white matter of brain. The dotted lines represent the sample axis.

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Abstract

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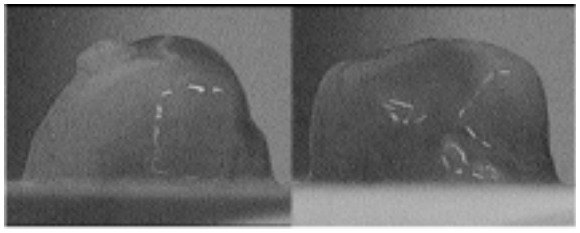

Fig. 2 : Typical sample from two perpendicular points of view.

B. Sample preparation

Seventeen samples were harvested from eight brains, and tested at a mean temperature of 28°C (27,3 ←→ 28,4°C). Brain mass was comprised between 82g and 102g, which is close to the weight of an adult swine. Pigs were sacrificed in a slaughtering house following standard procedures. The next day, brains were brought to the laboratory and placed into a refrigerator for not longer than 10h until testing.

Samples were harvested from brains using a biopsy punch (Stiefel, dia. 6mm), a standard cylindrical surgical tool. To prevent from brain adhesion the cutting tool was covered with special oil (Haribo®). Perpendicular samples were cut in parallel to the brain surface directly beneath gray matter. Parallel samples were cut perpendicular to the brain surface also directly beneath gray matter, one of their two faces tangential to gray matter. Location was randomly chosen, based on the assumption that there is no significant variation of white matter properties to be found in the brain [3]. After cutting a sample, the brain was replaced into the refrigerator until next sample cutting. Sizes of the samples were: height ≈ 4mm, width ≈ 5mm.

The cut sample was placed 15mn into a recipient filled with moist air, to attain 28°C without dehydration and to establish an equilibrated state which includes the geometry. A typical example of a sample from two perpendicular points of view is presented in Fig.2.

After the compression experiments samples exhibited no sign of dehydration.

C. Testing apparatus

For the testing apparatus (Fig. 3) we integrated a precision balance Ohaus® (model Adventurer, ± 0,001g) into a testing machine (G.T.Test®, model 108, precision = 0,5% of the read value for force and displacement). This solution was chosen to enable an excellent precision for elongation measurements provided by the testing machine, in conjunction with the high precision of the balance for very low load. Balance and compression plate were covered with oil (Haribo®) to prevent adhesion between testing apparatus and samples. A digital camera was integrated for evaluation of sample geometry and optical control during the experiment.

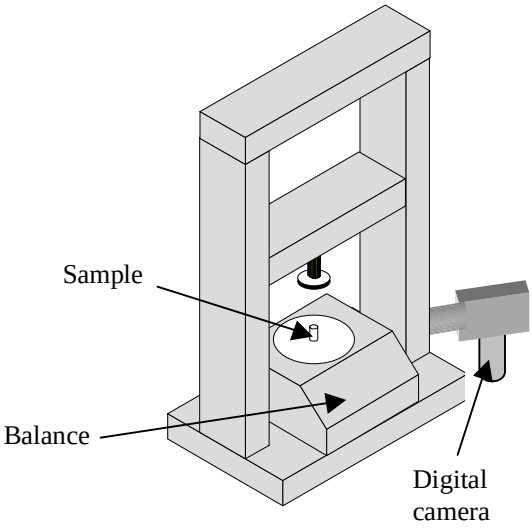

Fig. 3 : Schema of the testing apparatus

D. Compression protocol

Due to brain delicacy, no preconditioning was used. The experiment was performed under optical control of a digital camera. Low speed (0,007mm/mn) has been used to approach the sample.

Compression protocol : v = 0,5mm/mn, max. elongation = 1,5mm which corresponded to approximately 35% of the initial height of the samples. Load values were read out from the balance every 15 s ; one test lasted 3 mn.

III. RESULTS

Experimental results are presented in Fig. 4 as load vs. elongation curves of the medians of the experimental results. The shape of the curves was concave upward, which was already obtained by Miller and Chinzei [4].

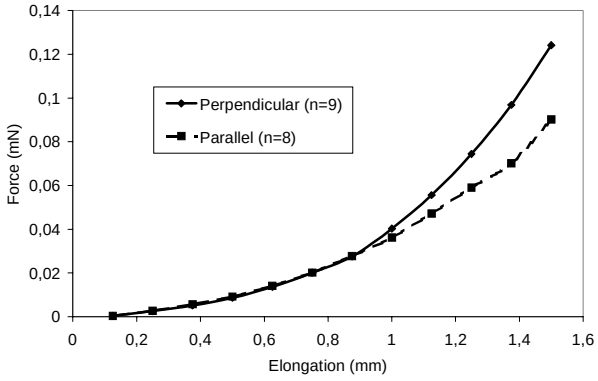

Fig. 4 : Load vs. elongation of medians for brain samples parallel and perpendicular to axons fibers

For an elongation of 0 to 25% white matter exhibited isotropy. For deformation superior to 25%, the load versus elongation curves diverged increasingly, just to a difference of 37% between the samples of the two perpendicular directions for 35% of elongation, respectively. For elevated elongation the perpendicular samples showed higher elasticity than the parallel ones.

IV. DISCUSSION

The samples evaluated under the described 'physiological' conditions kept due to their fragility unfortunately not their cylindrical shape but formed more or less cone like structures as shown in Fig. 2. That is the reason why we here have been able to investigate relative anisotropy only and could not quantify mechanical properties. Anyway since we took great care to perform all experiments under exactly the same circumstances it is possible to compare the results and determine relative values. This is what one needs to detect anisotropy.

To explain the initial isotropy of the white matter we may apply the following explanation given by Koeneman [1]: "When a force is applied the load is carried by the elastic forces of the compressed cells and intercellular (viscous) forces. As viscous forces are broken, an increasing amount of the load is carried by the cells which are further compressed". To transpose this hypothesis to our experiments on white matter : in the first phase load acts on intercellular medium and glial cells, before the axons are affected.

To explain the clear cut anisotropy found in higher elongation one has to take the histological structure of the tissue into account. Axons can be compared to very long tubes. If we hypothesize that at large deformations the adhesion qualities of the medium are lower (less adhesion forces due to glial cells), then it would be logical that compressing a mesh of long tubes perpendicularly to their axis requires more load than in parallel to them. Indeed in the second case axons would deform more easily.

V. CONCLUSION

Our results give clear cut evidence for anisotropy of the white matter of brain tissue *in vitro*. Under compression it shows an initial isotropic behavior, then becomes anisotropic for large deformations. This has to be taken into account in biomechanical simulation of brain tissue.

The method used to cut samples is based on histological literature.

Coupling high precision balance and a testing machine seems a good choice in quasistatic experiments : it is easy to use and allows very precise results at very low levels of load and displacements.

We are currently establishing new criteria to choose samples for analysis, and limit the problem due to a variation in the geometry of the samples.

To determine quantitative material properties also, we aim to develop an online evaluation of geometry of the samples under stress.

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